



THE UNIVERSITY *of* EDINBURGH

## Edinburgh Research Explorer

# Exome Sequencing to Detect Rare Variants Associated With General Cognitive Ability

### Citation for published version:

Generation Scotland 2015, 'Exome Sequencing to Detect Rare Variants Associated With General Cognitive Ability: A Pilot Study', *Twin Research and Human Genetics*, vol. 18, no. 2, pp. 117-125.  
<https://doi.org/10.1017/thg.2015.10>

### Digital Object Identifier (DOI):

[10.1017/thg.2015.10](https://doi.org/10.1017/thg.2015.10)

### Link:

[Link to publication record in Edinburgh Research Explorer](#)

### Document Version:

Peer reviewed version

### Published In:

Twin Research and Human Genetics

### Publisher Rights Statement:

© Luciano, M., Svinti, V., Campbell, A., Marioni, R. E., Hayward, C., Wright, A. F., ... Deary, I. J. (2015). Exome Sequencing to Detect Rare Variants Associated With General Cognitive Ability: A Pilot Study. *Twin Research and Human Genetics*, 1-9. [10.1017/thg.2015.10](https://doi.org/10.1017/thg.2015.10)

### General rights

Copyright for the publications made accessible via the Edinburgh Research Explorer is retained by the author(s) and / or other copyright owners and it is a condition of accessing these publications that users recognise and abide by the legal requirements associated with these rights.

### Take down policy

The University of Edinburgh has made every reasonable effort to ensure that Edinburgh Research Explorer content complies with UK legislation. If you believe that the public display of this file breaches copyright please contact [openaccess@ed.ac.uk](mailto:openaccess@ed.ac.uk) providing details, and we will remove access to the work immediately and investigate your claim.



# Exome Sequencing to Detect Rare Variants Associated With General Cognitive Ability: A Pilot Study

Michelle Luciano, Victoria Svinti, Archie Campbell, Riccardo E Marioni, Caroline Hayward, Alan F. Wright, Martin Taylor, David J Porteous, Pippa Thomson, James Prendergast, Nick Hastie, Susan Farrington, Generation Scotland, Malcolm Dunlop, Ian J Deary

## Supplementary Table S1

### Results From Gene Set Analysis for Significant Variants With Frequency <0.01

Obesity controls				Depression controls		
	Gene	Number of variants	<i>p</i> -value	Gene	Number of variants	<i>p</i> -value
All variants				<i>RP11-414H17.5</i>	2	1.34 <sup>-6</sup>
				<i>RP11-118B18.1</i>	2	1.97 <sup>-6</sup>
				<i>MESP2/SNORD113-9</i>	2	5.51 <sup>-6</sup>
Nonsynonymous	<b><i>SYNGAP1</i></b>	<b>3</b>	<b>4.0<sup>-6</sup></b>	<b><i>SYNGAP1</i></b>	<b>2</b>	<b>1.23<sup>-6</sup></b>
				<i>HOXD1/ HOXD-AS1</i>	2	8.82 <sup>-7</sup>
				<i>CECR6</i>	2	6.22 <sup>-7</sup>
				<i>AC022201.5</i>	2	1.04 <sup>-5</sup>
				<i>CYP26C1</i>	2	6.99 <sup>-6</sup>
				<i>ZNF703</i>	2	5.75 <sup>-7</sup>
				<i>NFKBIL1</i>	3	2.77 <sup>-5</sup>
Synonymous				<i>C9orf66</i>	2	1.92 <sup>-8</sup>
				<i>FAM110C</i>	2	3.91 <sup>-6</sup>
				<i>ID4/ RP1-167F1.2</i>	2	9.91 <sup>-6</sup>
				<i>TBC1</i>	2	3.44 <sup>-6</sup>

Note: Significant genes containing a single variant are not shown. Bold indicates common results across case-control subgroup analyses.

# Supplementary Table S2

## Results From Gene Set Analysis for Significant Variants With Frequency <0.05

Obesity controls				Depression controls		
	Gene	Number of variants	p-value	Gene	Number of variants	p-value
All variants	<b>RP11-673E1.4/ GYPB</b>	<b>14</b>	<b>2.74<sup>-12</sup></b>	<b>RP11-673E1.4/GYPB</b>	<b>11</b>	<b>9.94<sup>-7</sup></b>
	<b>/GYPA</b>	<b>/ 9</b>	<b>5.76<sup>-12</sup></b>	<b>/GYPA</b>	<b>/ 7</b>	<b>8.05<sup>-7</sup></b>
				RP11-414H17.5	2	1.16 <sup>-6</sup>
				RP11-118B18.1	2	1.08 <sup>-6</sup>
Nonsynonymous	<b>RP11-673E1.4/ GYPB</b>	<b>6</b>	<b>4.35<sup>-12</sup></b>	<b>RP11-673E1.4/ GYPB</b>	<b>5</b>	<b>2.85<sup>-7</sup></b>
	<b>/GYPA</b>	<b>/ 2</b>	<b>5.17<sup>-12</sup></b>	<b>/GYPA</b>	<b>/ 2</b>	<b>2.4<sup>-7</sup></b>
				CECR6	2	4.41 <sup>-8</sup>
				FAM136A/AC022201.5	2	4.62 <sup>-6</sup>
Synonymous				ZNF703	2	7.40 <sup>-7</sup>
				SOX17	2	2.61 <sup>-7</sup>
				FAM110C	2	4.16 <sup>-6</sup>
				ID4/RP1-167F1.2	2	9.35 <sup>-6</sup>

Note: Significant genes containing a single variant are not shown. Bold indicates common results across case-control subgroup analyses.

# Supplementary Table S3

## Significant Gene Ontology Pathways Enriched in the Varying Analyses Comprising the Depression Controls

	Gene ontology	<i>p</i> -value	FDR <i>p</i> -value	Enrichment values*	Genes in pathway
<b>Synonymous</b>					
SNVs<.01					
Molecular Function GO:0008376	acetylgalactosaminyl transferase activity	1.23E-5	.03	5.63 (6764,18,667,10)	<p><i>GALNT6</i> — udp-n-acetyl-alpha-d-galactosamine:polypeptide n-acetylgalactosaminyltransferase 6 (galnac-t6)</p> <p><i>GALNT12</i> — udp-n-acetyl-alpha-d-galactosamine:polypeptide n-acetylgalactosaminyltransferase 12 (galnac-t12)</p> <p><i>GALNT10</i> — udp-n-acetyl-alpha-d-galactosamine:polypeptide n-acetylgalactosaminyltransferase 10 (galnac-t10)</p> <p><i>B4GALNT3</i> — beta-1,4-n-acetyl-galactosaminyl transferase 3</p> <p><i>GALNT18</i> — udp-n-acetyl-alpha-d-galactosamine:polypeptide n-acetylgalactosaminyltransferase 18</p> <p><i>GALNT3</i> — udp-n-acetyl-alpha-d-galactosamine:polypeptide n-acetylgalactosaminyltransferase 3 (galnac-t3)</p> <p><i>GALNT2</i> — udp-n-acetyl-alpha-d-galactosamine:polypeptide n-acetylgalactosaminyltransferase 2 (galnac-t2)</p> <p><i>CHPF</i> — chondroitin polymerizing factor</p> <p><i>B3GALNT2</i> — beta-1,3-n-acetylgalactosaminyltransferase 2</p> <p><i>B4GALNT4</i> — beta-1,4-n-acetyl-galactosaminyl transferase 4</p>

Note: *p*-value, FDR corrected *p*-value, enrichment values, and prominent genes in each pathway are listed.

SNV: Single nucleotide variants\* Enrichment is defined as (b/n)/(B/N) [*N*: Total number of genes; *B*: Total number of genes associated with a specific GO term, *n*: Number of genes in the 'target set', *b*: Number of genes in the 'target set' associated with a specific GO term].